National consensus on Helicobacter pylori infection: the next-day challenge

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National consensus on *Helicobacter pylori* infection: the next-day challenge

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The Hellenic Society of Gastroenterology [1] recently published the National consensus on *Helicobacter pylori* (*H. pylori*) infection, following the necessity of a uniform approach to yield optimal eradication rates. As implied by the recent Maastricht V/Florence consensus [2], an "add-on" strategy regarding antibiotics was adapted to overleap the increasing antibiotic resistance, combined with the absence of bismuth-containing drugs, thus perpetuating a "vicious circle" and emerging novel approaches in treatment models with a targeted pathophysiological perspective. Importantly, parameters connected with the multidrug resistance include the formation of *H. pylori*-related biofilms, suggesting the introduction of novel anti-biofilm therapeutic approaches using anti-biofilm agents [3].

A unanimous suggestion (Statement 10) proposed that *H. pylori* culture or molecular techniques should be conducted to evaluate the antimicrobial susceptibility. Nevertheless, those methods are characterized by limited availability in most regions. On the other hand, recent data imply a potential benefit of vitamin D (vitD) for *H. pylori* infection treatment, related to the vitD-receptor's (VDR) antimicrobial role [4-6]. VDR, stimulated by the active *H. pylori* infection, induces human β-defensins, which in high concentrations suppress *H. pylori* biofilm activity [3]; subtle or strong activation of VDR, due to vitD absence or adequacy, could contribute or not to *H. pylori* acclimatization, morbidity, resistance, and survival [3]. Additionally, vitD seems to act directly as an antibacterial agent through stimulation of defensins and cathelicidins, and vitD upregulated protein 1 (VDP1). possesses an *H. pylori*-specific antimicrobial ability, indicating a promising therapeutic potential [7,8]. Moreover, studies in mouse models revealed a protective role of a VDP1 against *H. pylori*-related gastric cancer [9]. Clinical studies concluded that vitD had a protective role against *H. pylori* infection and suggested its deficiency as a distinct risk factor in the failure of eradication treatment, while a recent meta-analysis concluded that vitD supplementation could change the effectiveness of eradication regimens [10]. Therefore, a National multicenter study has recently been inaugurated to elucidate the relationship between vitD and *H. pylori* infection and the potential beneficial effect of vitD supplementation during eradication treatment.

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Authors' reply

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We read with great interest the letter by Papaefthymiou *et al* [1] concerning the Greek National Consensus on *Helicobacter pylori (H. pylori)* infection [2]. We certainly agree with the authors that over the past years in order to overcome the fast-growing antibiotic resistance of *H. pylori* infection worldwide, an "add-on" strategy has been adapted, and that this is more obvious in countries like Greece, where bismuth salts are not commercially available. Thus, novel *H. pylori* eradication regimens, with a more targeted pathophysiological approach, are under evaluation and we are awaiting with great interest the results of the ongoing clinical trials.

Eradication of *H. pylori* infection has traditionally relied on empiric therapeutic regimens, since the need for endoscopy and the limited availability of culture, in most countries including Greece, have rendered the susceptibility-guided treatment option impractical or even unfeasible. Moreover, a recent randomized study showed that susceptibility-guided therapy in a high-resistance area was equally effective as a local empirical regimen [3], while another randomized study failed to reveal superiority of genotypic resistance-guided therapy over a properly designed empirical treatment for eradication of refractory *H. pylori* infection [4]. For these reasons, the Greek consensus has stated (Statement 26) that culture and antimicrobial susceptibility testing is not recommended before first-line therapy, and that susceptibility-guided therapy should be provided as a rescue treatment, especially after second-line treatment has failed.

On the other hand, the effect of vitamin D (vitD) on *H. pylori* infection and eradication rates has been widely investigated recently [5]. VitD, apart from its well-known role in calcium and phosphorus metabolism, has been proven to be potent immune modulator of the adaptive immune system, stimulating the innate immune response upon infection [6]. Based on these data, several clinical studies have illustrated that vitD analogs may have anti-*H. pylori* antimicrobial effects. Cytological research has also found that $vitD_3$ decomposition product 1 can lyse *H. pylori* bacterial cells by inducing the collapse of the cell membrane [7]. However, the correlation with vitD has not been fully clarified and studies of the impact of serum vitD levels on *H. pylori* eradication were mostly observational or retrospective and of small sample size [8-10]. Therefore, well-designed randomized controlled prospective studies with a large sample size are needed. We were delighted to hear that a national multicenter study on the relationship between vitD and *H. pylori* was recently launched and we are awaiting the results.

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